FluMist® Update

Influenza Vaccine Summit Meeting
Atlanta, GA
April 19, 2007
## Refrigerated FluMist® Launch for 2007-08

<table>
<thead>
<tr>
<th>Regulatory Status &amp; Age Indication</th>
<th>FluMist (Frozen Formulation) Seasonal Vaccine No Longer Manufactured*</th>
<th>FluMist (Refrigerated Formulation) 2007/2008 Launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Storage</td>
<td>Licensed in U.S. in 2003 Healthy persons aged 5 – 49 years</td>
<td>Licensed in U.S. in 2007 Healthy persons aged 5 – 49 years</td>
</tr>
<tr>
<td></td>
<td>-15° C Freezer</td>
<td>2-8° C Refrigerator</td>
</tr>
<tr>
<td>Excipients</td>
<td>SPG</td>
<td>SPG, arginine, hydrolyzed porcine gelatin</td>
</tr>
<tr>
<td>Preservatives</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Dose Volume</td>
<td>0.5mL (0.25mL per nostril)</td>
<td>0.2mL (0.1mL per nostril)</td>
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</tbody>
</table>

*Frozen formulation may be used for pandemic vaccine.
Refrigerated FluMist®

- **Launch planned for 2007-08 season**
  - User stores vaccine refrigerated (2 - 8°C)
  - Current indication – healthy persons aged 5-49 years
  - Expanded indication for children aged 12-59 months without history of wheeze/asthma
    - Under FDA review
    - May 28 PDUFA date
  - Plan to manufacture 7 M doses

- **Pricing and Distribution**
  - Commercial – $17.95 per dose¹
    (AmerisourceBergen/McKesson)
  - VFC contract – $16.90 per dose¹ (project depots)

- **Availability targeted to begin in August**

¹ Excludes Federal Excise Tax
Impact of Expanded Recommendations
School-Aged Children

FluMist® Capacity
Update on Production of Vaccine

*Plasmid Rescue*

- Approved by FDA in 2006
- Alternate method for production of seasonal vaccine strains
- Required method for production of HPAI pandemic strains
Classical Reassortment

*Master Donor Virus*  
New Wild Type Strain

Co-infect cells

256 possible combinations

Six genes from MDV for *ca*,*ts*,*att*

Hemagglutinin and neuraminidase genes from wild type for immunity

6:2 Vaccine Seed Strain
Plasmid Rescue

**Master Donor Virus Plasmids**

- PB1
- NP
- PA
- PB2
- M
- NS

**New Wild Type Strain Plasmids**

- HA
- NA

Electroporate Vero cells

Only one possible combination

Six genes from MDV for ca, ts, att

Hemagglutinin and neuraminidase genes from wild type for immunity

6:2 Vaccine Seed Strain
Advantages of Plasmid Rescue

- **No genetic modifications introduced**
  - Same vaccine seeds as classical reassortment method
  - RNA sequence equivalent to classical reassortant

- **Further advantages**
  - Removes risk of exposure to adventitious agents in the wild type isolate
  - Fewer random mutations observed
  - Identical bulk production process

- **Timing of plasmid rescue is predictable**
  - Manufacturing can begin earlier, extending campaign
  - Earlier release of vaccine to the end user
  - Allows for greatest number of vaccine doses delivered